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# Vitamin D deficiency in adults - treatment and prevention

Last revised in September 2018    Next planned review by December 2021

## Changes

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**September 2018** – minor update. Recommendation on who to treat changed to be in line with SACN guidelines [[SACN, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].

**December 2016** – minor update.

- Ergocalciferol 1.25 mg (50,000 IU) capsules has been added to the section on product availability [[ABPI, 2016a \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].
- Desunin® (colecalciferol) 100 micrograms (4,000 IU) tablets has been added to the section on product availability [[BNF 72, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].

**August to November 2016** – this is a new CKS topic. The evidence base has been reviewed in detail, and recommendations are clearly justified and transparently linked to the supporting evidence.

## Update

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### New evidence

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### Evidence-based guidelines

- NOS (2018) *Vitamin D and bone health in adults*. National Osteoporosis Society. [www.nos.org.uk](http://www.nos.org.uk) (<https://nos.org.uk/>) [[Free Full-text \(https://nos.org.uk/for-health-professionals/tools-resources/#\)](#)]
- Specialist Pharmacy Service (2019) Which oral vitamin D dosing regimens correct deficiency in pregnancy? Specialist Pharmacy Service. [www.sps.nhs.uk](http://www.sps.nhs.uk) (<https://www.sps.nhs.uk/>) [[Free Full-text \(https://www.sps.nhs.uk/articles/which-oral-vitamin-d-dosing-regimens-correct-deficiency-in-pregnancy/\)](#)]

### HTAs (Health Technology Assessments)

No new HTAs since 1 October 2016.

### Economic Appraisals

No new economic appraisals relevant to England since 1 October 2016.

### Systematic reviews and meta-analyses

No new systematic reviews or meta-analysis since 1 October 2016.

### Primary evidence

No new randomized controlled trials published in the major journals since 1 October 2016.

### New policies

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No new national policies or guidelines since 1 October 2016.

### New safety alerts

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No new safety alerts since 1 October 2016.

- Colecalciferol 800 IU Film-coated tablets licensed for use in adults, elderly and adolescents for treatment of vitamin D deficiency, prevention of deficiency in high-risk patient, and as adjunct to specific therapy for osteoporosis in patients with vitamin D deficiency or at risk of vitamin D insufficiency. See the manufacturer's summary of product characteristics <http://www.medicines.org.uk/emc/medicine/32866> (<http://www.medicines.org.uk/emc/medicine/32866>).
- Colecalciferol 25,000 IU soft capsules are licensed for prophylaxis and treatment of vitamin D deficiency in adolescents and adults with an identified risk, and also as an adjunct to specific therapy for osteoporosis in patients with vitamin D deficiency or at risk of vitamin D insufficiency. See the manufacturer's summary of product characteristics <http://www.medicines.org.uk/emc/medicine/33710> (<http://www.medicines.org.uk/emc/medicine/33710>).

## Goals

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To support primary healthcare professionals to:

- Diagnose and manage vitamin D deficiency in adults.
- Prevent vitamin D deficiency (and associated risks) in adults.

## Outcome measures

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No outcome measures were found during the review of this topic.

## Audit criteria

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No audit criteria were found during the review of this topic.

## QOF indicators

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No QOF indicators were found during the review of this topic.

## QIPP - options for local implementation

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No QIPP indicators were found during the review of this topic.

## NICE Quality Standards

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No NICE quality standards were found during the review of this topic.

## What is it?

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- Vitamin D is a fat soluble vitamin that regulates calcium and phosphate homeostasis and is therefore vital for musculoskeletal health. It promotes the absorption of calcium and phosphorus from the bowel and enables mineralization of newly formed osteoid tissue in bones.
  - Vitamin D has also been associated with several non-musculoskeletal health outcomes (such as preventing cancer and cardiovascular disease), but the evidence for these is limited, conflicting, or absent. See the section on [Complications \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!backgroundSub:5\)](#) for more information.
- There are two main forms of vitamin D: vitamin D<sub>3</sub> (cholecalciferol) and vitamin D<sub>2</sub> (ergocalciferol).
  - Vitamin D<sub>3</sub> is synthesized in the skin from 7-dehydrocholesterol (7-DHC — a form of cholesterol naturally found in the skin) by the action of sunlight containing ultraviolet B (UVB) radiation (or by artificial UVB light).
  - Both vitamin D<sub>3</sub> and D<sub>2</sub> can be obtained from natural foods, fortified foods, and food supplements.
    - There are few natural rich food sources of vitamin D and most contain vitamin D<sub>3</sub>. Rich sources include cod liver oil (this also contains vitamin A which can be harmful in high doses and should be avoided in pregnancy) and oily fish (such as salmon, mackerel, and sardines). Egg yolk, meat, offal, milk, and mushrooms contain small amounts.
    - Vitamin D-fortified foods include fat spreads and some breakfast cereals and yoghurts.
    - Vitamin D<sub>3</sub> supplements are synthesized by UVB irradiation of 7-DHC from sheep wool, and vitamin D<sub>2</sub> by UVB irradiation of ergosterol from fungi.
- Dietary and cutaneous vitamin D are biologically inactive and require enzymatic conversion to the active metabolite 1, 25-hydroxyvitamin D (1,25[OH]<sub>2</sub>D).
  - Vitamin D is converted in the liver to 25-hydroxyvitamin D (25[OH]D), the main circulating metabolite. This is then converted to 1,25(OH)<sub>2</sub>D in the kidneys and other tissues.
  - The production of 1,25(OH)<sub>2</sub>D is regulated by the action of the parathyroid hormone (PTH) on the kidneys: a rise in PTH levels stimulates the synthesis of 1,25(OH)<sub>2</sub>D and vice versa.
- The best indicator of vitamin D exposure (from the diet and sunlight) is the serum concentration of 25(OH)D. This is because it has a long half-life in the circulation (about 2–3 weeks) and is not subject to tight homeostatic control. As a result, it provides an indication of vitamin D availability over

recent weeks.

- Serum 1,25(OH)<sub>2</sub>D concentration is not a suitable indicator of vitamin D exposure because it has a short half-life (less than 4 hours); it is homeostatically regulated; the plasma concentrations are not directly regulated by vitamin D intake (but by other factors, such as plasma PTH levels); and even in the presence of severe vitamin D deficiency, plasma concentrations may be normal or even elevated as a result of upregulation of cytochrome P450 27B1 (the enzyme which catalyzes the hydroxylation of 25(OH)D to 1,25(OH)<sub>2</sub>D).
- There is no clear consensus on the threshold serum 25(OH)D concentration used to define vitamin D deficiency in adults.
  - In agreement with the Institute of Medicine (IOM), the National Osteoporosis Society (NOS) propose the following thresholds in respect to bone health [National Osteoporosis Society, 2013 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]:
    - Less than 30 nmol/L – deficient.
    - 30–50 nmol/L – may be inadequate for some people.
    - Greater than 50 nmol/L – sufficient for most people.
  - Evidence identified by the Scientific Advisory Committee on Nutrition (SACN) suggests that the risk of poor musculoskeletal health is increased at serum 25(OH)D concentration below 25 nmol/L [SACN, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]. See the section on [Prevention of vitamin D deficiency](#) ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!scenario:1](#)) for more information.

[National Osteoporosis Society, 2013 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#)); PHE and FSA, 2014a ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#)); BMJ, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#)); NICE, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#)); SACN, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]

## What causes vitamin D deficiency in adults?

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- Vitamin D deficiency is most commonly caused by insufficient exposure to sunlight (which is the main source of vitamin D for most humans).
  - The amount of vitamin D synthesized in the skin depends on skin exposure to solar ultraviolet B (UVB) radiation (wavelength 280–315 nm) [SACN, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]. This can be affected by:
    - Season, time of day, and weather conditions – solar UV levels are highest in the UK summer months (between March and October) and around midday (between 11am and 3pm), but are reduced by cloud cover [NICE, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#)); SACN, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
    - Latitude – UVB radiation is sufficient for year round vitamin D synthesis at latitudes below 37° N (for example in Athens, Seville, and Sicily). At higher latitudes (including all of the UK), vitamin D is not synthesized in the winter months. However, the extent of the effect of latitude on vitamin D synthesis in the UK summer months may be relatively small compared with other factors.
    - Habit of dressing – wearing clothes that cover the entire body and face reduces skin exposure to sunlight.
    - Sunscreen use – some experts suggest that heavy sunscreen use reduces vitamin D production [BMJ, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#)); SACN, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]. However, evidence identified by the Scientific Advisory Committee on Nutrition (SACN) suggests that although sunscreens can significantly reduce the production of vitamin D under very strictly controlled conditions, their normal usage does not generally prevent vitamin D synthesis [SACN, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
  - The amount of vitamin D synthesized in the skin also depends on the efficiency of cutaneous synthesis. This can be affected by:
    - Age – lower serum 25-hydroxyvitamin D (25(OH)D) concentrations have been reported in older people compared with younger people. This is possibly because the amount of 7-dehydrocholesterol (7-DHC) present in the skin decreases with increasing age (the age at which this becomes a limiting factor if there is adequate sunlight exposure is unclear). It has also been suggested that the low 25(OH)D levels could be due to the fact that older people tend to wear more clothes, spend more time indoors, and are more likely to develop conditions that can affect the activation or bioavailability of vitamin D (such as reduced kidney or liver function).
    - Having darker skin – melanin, the pigment that gives skin its brown or black colour, absorbs a proportion of the UVB radiation needed for cutaneous synthesis of vitamin D. People with dark skin may therefore need more sunlight exposure to produce the same amount of vitamin D as people with lighter skin [NICE, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
- Other possible causes of vitamin D deficiency include:
  - Inadequate dietary and supplemental vitamin D
    - In the winter months in the UK (from October to March), sunlight contains very little of the UVB needed to synthesize vitamin D. It therefore has to be obtained from body stores (from UVB exposure in the summer months) and dietary sources, including natural foods, fortified foods, and food supplements.
    - It is difficult to get enough vitamin D from [food sources](#) ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!backgroundSub](#)) alone because they are limited and often do not contain enough vitamin D to satisfy daily requirements.
  - Conditions that impair the absorption of vitamin D
    - Intestinal malabsorption syndromes (such as coeliac disease, cystic fibrosis, and Crohn's disease) impair the absorption of dietary vitamin D, leading to decreased bioavailability.
    - Obesity (body mass index [BMI] greater than 30 kg/m<sup>2</sup>) is associated with lower vitamin D levels, although the reason is unclear. One theory is that because vitamin D is fat soluble and is readily stored in adipose tissue, it could be sequestered in body fat compartments of obese people, leading to reduced bioavailability [Wortsman et al, 2000 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#)); Vanlint, 2013 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#)); BMJ, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
    - Severe liver failure is associated with fat malabsorption [BMJ, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
  - Conditions that impair the activation of vitamin D
    - Chronic kidney disease (CKD) or kidney failure impairs the production of sufficient 1,25-dihydroxyvitamin D (1,25(OH)<sub>2</sub>D).
    - Liver disease can also impair the activation of vitamin D. When more than 90% of the liver fails, it is incapable of producing enough 25-hydroxyvitamin D (25(OH)D) [BMJ, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].

- Inherited enzyme disorders are rare and include mutation of renal 25-hydroxyvitamin D 1 alpha-hydroxylase (which causes pseudovitamin D-deficiency rickets).
- Other conditions
  - Nephrotic syndrome can cause urinary loss of vitamin D.
  - Cancers (malignant or benign) can cause hypophosphataemia and low levels of serum 1,25(OH)<sub>2</sub>D.
- Certain drugs
  - Drugs that reduce fat absorption (for example orlistat) can lead to a decreased bioavailability of vitamin D [Preston, 2015 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references)].
  - Antiepileptic drugs (especially carbamazepine, phenobarbital, and phenytoin), colestyramine, rifampicin, corticosteroids, and highly active antiretroviral treatment (HAART) can actively destroy vitamin D by activating the catabolism of both 25(OH)D and 1,25(OH)<sub>2</sub>D.
  - See the section on [Drug interactions \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!prescribingInfoSub:4\)](#) for more information.

[Bordelon et al, 2009 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references); Pearce and Cheetham, 2010 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references); Hull and Anastasiadis, 2011 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references); BMJ, 2016 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references); SACN, 2016 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references); NICE, 2016 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references)]

## Who is at higher risk of vitamin D deficiency?

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- In the UK, people at higher risk of vitamin D deficiency include those:
  - With limited sun exposure, for example people who:
    - Cover up their skin for cultural reasons (for example Muslim women) or for health reasons (for example people with skin photosensitivity or a history of skin cancer).
    - Spend very little time outdoors (for example those who are housebound or institutionalized).
  - With dark skin (for example those of African, African-Caribbean, or Asian or Middle-Eastern ethnic origin).
- Vitamin D deficiency can also occur in people who:
  - Are at increased risk of nutritional deficiency, for example vegans and those who do not eat fish, or generally have a poor diet.
  - Are pregnant or breastfeeding.
  - Are elderly (65 years and older).
  - Have certain [conditions \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!backgroundSub:1\)](#) (such as a malabsorption syndrome) or are taking certain [drugs \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!backgroundSub:1\)](#) (such as some antiepileptic drugs) that may increase the risk of vitamin D deficiency.
  - Are obese (body mass index greater than 30 kg/m<sup>2</sup>) or have had gastric bypass surgery.
  - Have a family history of vitamin D deficiency.

[Kennel et al, 2010 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references); Pearce and Cheetham, 2010 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references); Pearce et al, 2011 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references); DH, 2012 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references); BMJ, 2016 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references); NICE, 2016 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references); SACN, 2016 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references)]

## How common is it?

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- Vitamin D deficiency is the most common nutritional deficiency in the world. It affects people of all ages, especially if there are [risk factors \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!backgroundSub:2\)](#) [BMJ, 2016 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references)].
- The [National Diet and Nutrition Survey \(https://www.gov.uk/government/statistics/national-diet-and-nutrition-survey-results-from-years-1-to-4-combined-of-the-rolling-programme-for-2008-and-2009-to-2011-and-2012\)](https://www.gov.uk/government/statistics/national-diet-and-nutrition-survey-results-from-years-1-to-4-combined-of-the-rolling-programme-for-2008-and-2009-to-2011-and-2012) (which is designed to assess the diet, nutrient intake, and nutritional status of the general UK population aged 1.5 years and over living in private households) reported low vitamin D status, as indicated by serum 25-hydroxyvitamin D (25(OH)D) concentrations below 25 nmol/L, in people of all age groups [PHE and FSA, 2014a (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references); PHE and FSA, 2014b (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references)]:
  - Over the year as a whole, combined results from a four-year rolling programme (2008/2009 – 2011/12) showed low vitamin D levels in 23% of people aged 19–64 years and 21% of people aged 65 years and over. In the months of January to March, this increased to 30% of people aged 65 years and over and 40% of people aged 19–64 years.

## What is the prognosis?

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- Management of vitamin D deficiency and correction of [risk factors \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!backgroundSub:2\)](#) (where possible) should:
  - Restore vitamin D levels.
  - Reduce the risk, or improve the symptoms, of [complications \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!backgroundSub:5\)](#), such as osteomalacia, falls, and muscle weakness.
- Following treatment for vitamin D deficiency or insufficiency, people will require lifestyle changes in addition to daily vitamin D supplement, including in the winter months, to maintain optimum vitamin D levels.

## What are the complications of vitamin D deficiency?

- The complications of vitamin D deficiency are largely musculoskeletal.
  - The main complication of vitamin D deficiency in adults is osteomalacia [[National Osteoporosis Society, 2013 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].
    - Prolonged vitamin D deficiency results in the skeleton becoming the body's main source of calcium, with osteoclasts breaking down bone to raise serum calcium. This leads to osteomalacia, which may precipitate or exacerbate osteopenia and osteoporosis [[Bordelon et al, 2009 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#); [Smith and Wordsworth, 2010 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].
  - Less severe vitamin D deficiency (or vitamin D insufficiency) may lead to hypocalcaemia, secondary hyperparathyroidism, bone loss, muscle weakness, and falls and fragility fractures in older people [[National Osteoporosis Society, 2013 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].
  - Except for the above mentioned, vitamin D deficiency has not been convincingly related to other musculoskeletal symptoms in adults.
- Vitamin D deficiency has also been associated with several non-musculoskeletal complications, but the evidence for these are inconsistent, conflicting, or absent [[NICE, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#); [SACN, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].
  - The Scientific Advisory Committee on Nutrition (SACN) reviewed the evidence on a number of health outcomes associated with vitamin D to assess whether any might be used to inform the setting of Dietary Reference Values (DRVs) for vitamin D [[SACN, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].
  - There was insufficient evidence from non-musculoskeletal health outcomes (including reproductive health [on maternal and newborn outcomes], cancers, cardiovascular disease, hypertension, all-cause mortality, immune modulation, infectious diseases, neuropsychological functioning, age-related macular degeneration, and oral health) to inform the setting of DRVs. However, the evidence on musculoskeletal health outcomes (osteomalacia, falls, and muscle strength and function) was considered to be suggestive of a beneficial effect of vitamin D and was therefore used as the basis for setting the DRVs.
  - See the section on [Prevention of vitamin D deficiency \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!scenario:1\)](#) for more information.

## Who should I test for vitamin D deficiency?

- Do not routinely test for vitamin D deficiency.
- Test for vitamin D deficiency, by measuring serum 25-hydroxyvitamin D (25(OH)D) levels, if a person presents with the following, especially if they are at [higher risk \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!backgroundSub:2\)](#) of vitamin D deficiency:
  - Symptoms of osteomalacia, such as:
    - Bone discomfort or pain (often throbbing) in lower back, pelvis, and lower extremities.
    - Impaired physical function.
    - Muscle aches and weakness – this may be marked, is usually most noticeable in the quadriceps and glutei, and can result in difficulty in rising from a seating position, or a waddling gait.
    - Symmetric lower back pain.
  - Chronic widespread pain.
- Also test for vitamin D deficiency if there is a clinical reason to do so, for example:
  - Prior to specific treatment where correcting vitamin D deficiency is appropriate.
  - If the person has a bone disease that may be improved with vitamin D treatment, such as osteomalacia, osteoporosis, or Paget's disease.
  - If the person has had a fall.
  - If the person has features of hypocalcaemia (rare), including muscle cramps, carpopedal spasm, numbness, paraesthesias, tetany, or seizures.

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### Basis for recommendation

### Who to test

- The recommendation on who to test is based on expert opinion in the National Osteoporosis Society (NOS) guideline *Vitamin D and bone health: a practical clinical guideline for patient management* [[National Osteoporosis Society, 2013 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)] and the National Institute for Health and Care Excellence (NICE) guideline *Vitamin D: increasing supplement use in at-risk groups* [[NICE, 2014 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].
  - NOS recommends testing people for whom the outcome will alter clinical management, including people with [[National Osteoporosis Society, 2013 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)]:
    - Bone diseases that may be improved with vitamin D treatment – NOS found good evidence that correcting vitamin D deficiency is essential in osteomalacia and may be beneficial in osteoporosis.
    - Bone diseases, prior to specific treatment where correcting vitamin D deficiency is appropriate – NOS recognizes that there are bone diseases (such as Paget's disease) for which correcting vitamin D deficiency is recommended before drug treatment. It is also important that people receiving potent antiresorptive osteoporosis treatments (denosumab or zoledronate) are not vitamin D deficient before starting treatment, to reduce the risk of developing hypocalcaemia.
    - Musculoskeletal symptoms that could be attributed to vitamin D deficiency – NOS states that although the symptoms of vitamin D deficiency are vague and it can be difficult to ascertain whether a low serum 25(OH)D level is causal or a surrogate marker (for example of poor nutrition or a

lack of outdoor activity), it is reasonable to test people suspected of having symptoms caused by osteomalacia and people who have chronic widespread pain.

- NICE recommends testing if there are symptoms of vitamin D deficiency and if there is a clinical reason to do so (for example osteomalacia or a fall) [[NICE, 2014 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)]. NICE also recommends testing vitamin D levels in people who are considered to be at very high risk of vitamin D deficiency (for example those with very low exposure to sunlight). However, the Scientific Advisory Committee on Nutrition (SACN) report *Vitamin D and health*, which NICE advises their guideline should be used in conjunction with, recommends daily vitamin D supplements for all people in the UK, including people thought to be at increased risk of vitamin D deficiency, but does not recommend vitamin D testing *prior* to supplementation [[SACN, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].
- Although uncommon, symptoms of hypoglycaemia are also diagnostic factors for vitamin D deficiency [[BMJ, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].

#### How to test

- Experts agree that measuring serum 25-hydroxyvitamin D (25[OH]D) is the best indicator of vitamin D status. This is because it reflects cutaneous and dietary sources of vitamin D, has a fairly long half-life (2–3 weeks), and is not subject to tight homeostatic control. As a result, it gives an indication of vitamin D availability over recent weeks [[NICE, 2014 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#); [National Osteoporosis Society, 2013 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#); [BMJ, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#); [SACN, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].

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## How should I diagnose vitamin D deficiency in adults?

- Diagnose vitamin D deficiency if serum 25-hydroxyvitamin D (25[OH]D) levels are less than 25 nmol/L.
  - Consider arranging the following investigations (depending on clinical presentation and clinical judgment to aid the diagnosis of vitamin D deficiency and to exclude [differential diagnoses \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!diagnosisSub:2\)](#)):
    - Bone profile (calcium, phosphate, and alkaline phosphatase [ALP]), to assess for hypocalcaemia and markers of bone disease.
    - Renal, liver, and thyroid function tests.
    - Parathyroid hormone (PTH) levels.
    - Full blood count, including haemoglobin and ferritin levels (to identify other possible vitamin deficiencies).
    - Malabsorption screen.
    - Rheumatoid and other autoimmune screening.
    - Inflammatory markers (erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP], to exclude other inflammatory disorders).
- Serum 25(OH)D levels in the range of 25–50 nmol/L may be inadequate for some people.
- Serum 25(OH)D levels greater than 50 nmol/L are sufficient level for most people.

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#### Basis for recommendation

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#### Diagnosis of vitamin D deficiency

- The recommendation on when to diagnose vitamin D deficiency is based on expert opinion in the Scientific Advisory Committee on Nutrition (SACN) guideline *Vitamin D and health* [[SACN, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].

#### Considering investigations

- This recommendation (and the recommended investigations) is based on expert opinion in local vitamin D guidelines issued by the Barts and The London School of Medicine and Dentistry [[Hull and Anastasiadis, 2011 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)], the Public Health and Management teams at NHS Camden Clinical Commissioning Group [[Camden Clinical Commissioning Group NHS, 2014 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)], and Coventry and Warwickshire Area Prescribing Committee [[Coventry & Warwickshire Area Prescribing Committee, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)], expert opinion in a review article on vitamin D deficiency [[BMJ, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)], and on what CKS considers to be good clinical practice.

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## What else might it be?

- Conditions that may present with bone pain and/or muscle weakness include:
  - Certain cancer, including:
    - Bone cancer — increasing, unexplained, or persistent bone pain or tenderness, particularly at rest (and especially if not in the joint); swelling; and unexplained limp. See the CKS topic [Bone and soft tissue sarcoma - recognition and referral \(/bone-and-soft-tissue-sarcoma-recognition-and-referral\)](#) for more information.
    - Soft tissue sarcoma — palpable fixed or immobile lump that is increasing in size. See the CKS topic on [Bone and soft tissue sarcoma - recognition and referral \(/bone-and-soft-tissue-sarcoma-recognition-and-referral\)](#) for more information.
    - Myeloma — weakness, fatigue, bone pain, and, less commonly, renal failure, hypercalcaemia, and acute infection. See the CKS topic on [Multiple myeloma \(/multiple-myeloma\)](#) for more information.
  - Fibromyalgia — pain associated with generalized morning stiffness and worsened by stress, cold, and activity.
  - Fracture — pain, swelling, or bruising over a bone, and deformity.
  - Osteomyelitis — variable pain and disability, possible evidence of soft tissue swelling and bony tenderness, and systemic features (such as weight loss and malaise).

- Paget's disease of the bone — dull pain aggravated by weight bearing; bowing of weight bearing bones (especially tibia, femur, and forearm [usually asymmetrical]); mostly occurs in elderly men.
- Parathyroid disease (hyperparathyroidism causing hypercalcaemia) — bone pain, muscular weakness, gastrointestinal symptoms (such as anorexia and nausea), renal stones, cardiac arrhythmias, and neurological symptoms (such as depression and confusion).
- Polymyalgia rheumatica — bilateral shoulder and/or pelvic girdle pain and stiffness lasting for at least 45 minutes after waking or periods of rest; usually occurs in people aged over 50 years of age. See the CKS topic on [Polymyalgia rheumatica \(/polymyalgia-rheumatica\)](#) for more information.
- Rheumatoid arthritis — pain, swelling, and heat in the affected joints. See the CKS topic on [Rheumatoid arthritis \(/rheumatoid-arthritis\)](#) for more information.
- Conditions that may present with painless muscle weakness include:
  - Polymyositis and dermatomyositis — may also present with cutaneous changes in dermatomyositis and increased serum creatine kinase.
  - Thyroid disease — presents with a wide range of symptoms and signs, including tiredness and weakness. See the CKS topics on [Hyperthyroidism \(/hyperthyroidism\)](#) and [Hypothyroidism \(/hypothyroidism\)](#) for more information.
  - Muscular dystrophies — progressive degeneration and weakness of some muscle groups.

Basis for recommendation

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This information is based on expert opinion in review articles [[Salvarani et al, 2002 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#); [Salvarani et al, 2008 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#); [Weetman, 2010 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#); [BMJ, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)], the Oxford textbook of medicine [[Berendt and McNally, 2010 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)], and the Oxford handbook of General Practice [[Simon et al, 2010 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].

## Scenario: Management of vitamin D deficiency or insufficiency in adults

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From age 18 years onwards.

Who should be treated for vitamin D deficiency or insufficiency?

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- [Treat \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!scenarioRecommendation:1\)](#) for vitamin D deficiency if serum 25-hydroxyvitamin D (25[OH]D) levels are less than 25 nmol/L.
- [Treat \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!scenarioRecommendation:1\)](#) for vitamin D insufficiency if serum 25(OH)D levels are in the range of 25–50 nmol/L and the person:
  - Has a fragility fracture, documented osteoporosis, or high fracture risk.
  - Is being treated with an antiresorptive drug for bone disease.
  - Has [symptoms \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!diagnosisSub\)](#) suggestive of vitamin D deficiency.
  - Is at [increased risk \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!backgroundSub:2\)](#) of developing vitamin D deficiency in the future, for example because of reduced sunlight exposure.
  - Has raised parathyroid hormone levels.
  - Is taking an antiepileptic drug or an oral corticosteroid, or is on long-term treatment with other [drugs \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!backgroundSub:1\)](#) known to cause vitamin D deficiency, such as colestyramine.
  - Has a malabsorption disorder (for example Crohn's disease) or other [condition \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!backgroundSub:1\)](#) known to cause vitamin D deficiency, such as chronic kidney disease.
- If serum 25(OH)D levels are adequate (that is, above 50 nmol/L), advise on [measures to prevent vitamin D deficiency \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!scenario:1\)](#).
  - If the person has musculoskeletal symptoms (such as muscle pain or weakness) despite adequate serum 25(OH)D levels, consider an [alternative diagnosis \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!diagnosisSub:2\)](#).

Basis for recommendation

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This recommendation is largely based on the National Osteoporosis Society (NOS) guideline *Vitamin D and bone health: a practical clinical guideline for patient management* [[National Osteoporosis Society, 2013 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)] and Scientific Advisory Committee on Nutrition (SACN) guideline *Vitamin D and Health* [[SACN, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].

- CKS and NOS recommend treating people with serum 25-hydroxyvitamin D (25[OH]D) levels in the range of 25–50 nmol/L who are taking an antiepileptic drug or an oral corticosteroid. Based on good clinical practice, CKS recommends also treating people on long-term treatment with other drugs known to cause vitamin D deficiency.
- CKS and NOS recommends treating people with 25(OH)D levels in the range of 25–50 nmol/L who have a malabsorption disorder. Based on good clinical practice, CKS recommends also treating people with other conditions known to cause vitamin D deficiency.
- The recommendation to consider an alternative diagnosis if there are musculoskeletal symptoms at serum 25(OH)D above 50 nmol/L is extrapolated from expert opinion in the NOS vitamin D guideline for children and young people, which states that if a child or young person treated for vitamin D deficiency remains symptomatic despite satisfactory 25(OH)D concentrations, symptoms are unlikely to be related to vitamin D deficiency [[National Osteoporosis Society, 2015 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].

- Consider the need for referral or seeking specialist advice.
  - Refer to an appropriate specialist (using clinical judgement to decide on the urgency) if a serious underlying condition, such as cancer or a malabsorption disorder (for example Crohn's disease), is suspected. See the sections on [Causes](#) (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!backgroundSub:1) and [Differential diagnosis](#) (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!diagnosisSub:2).
  - Refer or seek specialist advice (depending on clinical judgement) if the person:
    - Has a fragility fracture, documented osteoporosis, or high fracture risk, or is being treated with an antiresorptive drug for bone disease.
    - Has raised parathyroid hormone levels.
    - Is taking an antiepileptic drug or an oral corticosteroid, or is on long-term treatment with other [drugs](#) (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!backgroundSub:1) known to cause vitamin D deficiency, such as colestyramine.
    - Has a malabsorption disorder (for example Crohn's disease) or other [condition](#) (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!backgroundSub:1) known to cause vitamin D deficiency, such as chronic kidney disease.
    - Has a co-existing condition associated with increased sensitivity to vitamin D (such as sarcoidosis, tuberculosis, lymphoma, or primary hyperparathyroidism).
    - Is a pregnant woman.
    - Has an unexplained deficiency.
- Choose the most appropriate vitamin D preparation for the person.
  - Vitamin D<sub>2</sub> is recommended for strict vegans as it is derived from plant sources. There are also vitamin D preparations for people with peanut or soya allergy and people with halal or kosher requirements.
  - See the section on [Available preparations](#) (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!prescribingInfoSub:2) for more information.
- Choose the most appropriate treatment regimen.
  - For the treatment of vitamin D deficiency, the recommended treatment is based on fixed loading doses of vitamin D (up to a total of about 300,000 international units [IU]) given either as weekly or daily split doses, followed by lifelong maintenance treatment of about 800 IU a day. Higher doses of up to 2000 IU a day, occasionally up to 4000 IU a day, may be used for certain groups of people, for example those with malabsorption disorders.
    - Several treatment regimens are available, including 50,000 IU once a week for 6 weeks (300,000 IU in total), 20,000 IU twice a week for 7 weeks (280,000 IU in total), or 4000 IU daily for 10 weeks (280,000 IU in total).
  - For the treatment of vitamin D insufficiency, maintenance doses should be started without the use of loading doses.
- Calculate dietary calcium intake.
  - Several online calcium calculators are available, such as the [Institute of Genetics and Molecular Medicine calcium calculator](#) (<http://www.cgem.ed.ac.uk/research/rheumatological/calcium-calculator>).
  - For people with inadequate calcium intake (less than 700 mg a day for most people or less than 1000 mg a day for people with osteoporosis) or people with confirmed hypocalcaemia, advise on dietary measures to correct this.
    - See the British Dietetic Association (BDA) factsheet on [calcium](#) (<https://www.bda.uk.com/foodfacts/Calcium.pdf>) (available at [www.bda.uk.com](http://www.bda.uk.com/) (<https://www.bda.uk.com/>)) for information on how the daily calcium intake can be achieved.
    - Dietary calcium deficiency is common in people with a low meat and milk product intake and may be significantly exacerbated where there is a high dietary intake of phytate (contained in chapatti flour, wholegrain, and wholemeal flour), which binds calcium in the intestine.
  - For people who are unable or unwilling to increase their dietary calcium, consider the need for [supplemental calcium](#) (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!prescribingInfoSub:6) (in addition to high-dose vitamin D) – consider seeking specialist advice.
  - Combined calcium and vitamin D preparations (such as Calcichew D3®) are available; however, they are not recommended for people on high-dose vitamin D treatment because they contain very low levels of vitamin D (200–400 IU per tablet) and may result in high dosing of calcium, thereby increasing the risk of hypercalcaemia.
- Advise the person:
  - To seek medical advice if they develop any [adverse effects](#) (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!prescribingInfoSub:3) during treatment with high-dose vitamin D, such as nausea and vomiting.
  - On [lifestyle measures](#) (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!scenarioRecommendation:2) to reduce the risk of recurrence.
- [Follow up](#) (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!scenarioRecommendation:3) the person to ensure that vitamin D deficiency/insufficiency has been treated and to assess for [vitamin D toxicity](#) (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!prescribingInfoSub:3) (although this is unlikely at the recommended doses).
  - Be aware that vitamin D treatment can unmask previously undiagnosed primary hyperparathyroidism.

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## Basis for recommendation

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These recommendations are largely based on the National Osteoporosis Society (NOS) guideline *Vitamin D and bone health: a practical clinical guideline for patient management* [National Osteoporosis Society, 2013 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references)], local vitamin D guidelines issued by the North of Tyne [Pearce et al, 2011 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references)], Barts and The London School of Medicine and Dentistry [Hull and Anastasiadis, 2011 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references)], and NHS Wales [NHS Wales, 2014 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references)], and expert opinion in review articles on vitamin D deficiency [Pearce and Cheetham, 2010 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references); BMJ, 2016 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references)].

## Arranging referral if a serious underlying cause is suspected

- This recommendation is based on what CKS considers to be good clinical practice.



## Arranging referral or seeking specialist advice in certain groups

- This recommendation aims to ensure that the appropriate dose, duration, and treatment regimen of vitamin D is given. For example:
  - People with malabsorption disorders or chronic liver disease would need higher doses of vitamin D (for example ergocalciferol tablets up to 40,000 international units [IU] a day) [BNF 72, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))], preferably given parenterally to improve absorption [Pearce and Cheetham, 2010 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#)); NHS Wales, 2014 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
  - People with kidney disease that is severe enough to impair the hydroxylation of vitamin D may require treatment with a short-acting, potent vitamin D analogue, such as alphacalcidol or calcitriol (specialist initiation only) [BNF 72, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
  - People with co-existing conditions associated with increased sensitivity to vitamin D are at increased risk of vitamin D toxicity and therefore need lower doses of vitamin D and more frequent monitoring [Hull and Anastasiadis, 2011 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))] [National Osteoporosis Society, 2013 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
  - The effect of high-dose vitamin D on pregnancy is unclear:
    - The UK teratology information services (UKTIS) states that there are insufficient data available in the literature to provide a detailed risk assessment of high-dose vitamin D treatment during pregnancy, but it should not be withheld if needed, considering the possible risks associated with poor maternal vitamin D status during pregnancy. However, other risk factors may be present in individual cases which may independently increase the risk of adverse pregnancy outcome. UKTIS states reminds clinicians of the importance of considering such factors when performing case-specific risk assessments [UKTIS, 2013 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]. Expert opinion of a reviewer of this CKS topic is that treating a 'possible risk' by giving high-dose vitamin D to pregnant women seems to be questionable.
    - The *Institute of Medicine (IOM): Dietary reference intakes for calcium and vitamin D* recommends a daily dose of 600 IU of vitamin D for pregnant and breastfeeding women, and states that a maximum daily dose of 4000 IU of vitamin D is safe during pregnancy and breastfeeding [IOM, 2010 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))] [Ross and Grahame, 2011 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
    - Expert opinion in the American Congress of Obstetricians and Gynecologists (ACOG) committee publication *Vitamin D: screening and supplementation during pregnancy* is that most experts agree that 1000–2000 IU of vitamin D a day is safe during pregnancy and breastfeeding. However, it was highlighted that the use of higher dose regimens for the treatment of vitamin D deficiency during pregnancy has not been studied [ACOG, 2011 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].

## Choosing the most appropriate vitamin D preparation

- NOS recommends vitamin D<sub>3</sub> as the preparation of choice for the treatment of vitamin D deficiency [National Osteoporosis Society, 2013 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
- The current consensus is that it raises serum vitamin D concentrations more effectively than vitamin D<sub>2</sub> (due to higher affinities for liver enzymes, plasma vitamin D binding protein, and vitamin D receptors) [UKMJ, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
  - Results from studies (identified by SACN) that compared the effectiveness of vitamin D<sub>2</sub> and vitamin D<sub>3</sub> in raising serum 25-hydroxyvitamin D (25[OH]D) concentrations have been inconsistent, but most of the evidence supports the suggestion that vitamin D<sub>3</sub> is more effective than vitamin D<sub>2</sub> in raising serum 25(OH)D concentrations [SACN, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
- Vitamin D<sub>2</sub> is recommended for strict vegans because it is derived from plant sources, unlike vitamin D<sub>3</sub> which is derived from animal sources [UKMJ, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].

## Choosing the most appropriate treatment regimen

- The recommendation on treating vitamin D deficiency is based on expert opinion in the NOS guideline [National Osteoporosis Society, 2013 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
  - NOS acknowledges that in theory, a titrated treatment approach is likely to be more effective than a fixed loading dose regime at restoring vitamin D levels and reducing the risk of vitamin D toxicity. However, these advantages do not outweigh the disadvantages of the increased costs of titration testing and the effect of increasing complexity on the prescriber and the person.
    - Loading with oral vitamin D is preferred to parenteral vitamin D for most people because there is evidence that vitamin D stores are replenished more rapidly with oral preparations, and bioavailability is more predictable.
  - The recommendation on treating vitamin D insufficiency is extrapolated from the NOS guideline, which states that where correction of vitamin D deficiency is less urgent, maintenance treatment may be started without the use of loading doses.

## Vitamin D treatments not routinely recommended

- Short-acting, potent vitamin D analogues (such as alphacalcidol and calcitriol) and annual depot vitamin D treatments (oral or parenteral) are not routinely recommended because they have been shown to cause toxicity or not to work [National Osteoporosis Society, 2013 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
- Short-acting, potent vitamin D analogues should only be prescribed in people with renal impairment that is severe enough to impair the hydroxylation of vitamin D to its active metabolite (specialist initiation only) [BNF 72, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
- Liquid 'special preparations' of vitamin D (unlicensed) are not routinely recommended for use in adults because more cost-effective alternatives are available [Hull and Anastasiadis, 2011 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].

## Ensuring adequate calcium intake

- Adequate levels of both vitamin D and calcium are needed to ensure optimum serum calcium levels, and it is important to ensure that both are maintained to prevent long-term adverse effects on the bones [BMJ, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
- The recommendation to consider the need for supplemental calcium only when an adequate dietary intake of calcium cannot be achieved is extrapolated from expert opinion in the National Osteoporosis Guideline Group (NOGG) guideline *Osteoporosis: clinical guideline for prevention and*

*treatment*, which states that it may be prudent to increase dietary calcium intake and use vitamin D alone where the use of calcium and vitamin D supplementation might otherwise be considered. In their expert opinion [NOGG, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]:

- Compliance and persistence with calcium-containing supplements is poor (possibly due to the unpalatability of the calcium component).
- High dietary calcium does not seem to carry the same increased risk of cardiovascular events as has been suggested for calcium supplements in several studies (although these studies have been widely criticised and the putative association requires further clarification).
- There are no preparations containing high-dose vitamin D in combination with calcium. NOS advises that the available calcium and vitamin D combination products (such as CalciChew-D<sub>3</sub>®) should not be used as sources of vitamin D for treating vitamin D deficiency because of the resulting high doses of calcium [National Osteoporosis Society, 2013 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
- The recommended dose of calcium (1–2 g) is in line with the Institute of Medicine (IOM)'s recommended dietary calcium allowance for adults aged 18 years and older [IOM, 2010 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].

#### Giving lifestyle advice

- This recommendation is based on expert opinion in the NOS guideline [National Osteoporosis Society, 2013 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))] and a review article on vitamin D deficiency [BMJ, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].

#### Following up to ensure vitamin D repletion and to assess for vitamin D toxicity

- This recommendation is based on expert opinion in the NOS guideline [National Osteoporosis Society, 2013 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))], a vitamin D guideline issued by Barts and The London School of Medicine and Dentistry [Hull and Anastasiadis, 2011 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))], and review articles on vitamin D deficiency [Pearce and Cheetham, 2010 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))] [BMJ, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
- The NOS guideline states that the aims of monitoring people on high-dose vitamin D treatment are to detect people [National Osteoporosis Society, 2013 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]:
  - Who remain deficient after loading.
  - Who become deficient during maintenance.
  - In whom vitamin D treatment uncovers sub-clinical primary hyperparathyroidism.
- Expert opinion in the Scientific Advisory Committee on Nutrition (SACN) report on *Vitamin D and health* is that vitamin D doses of 300,000 IU at intervals of 3 months or longer would not be expected to cause adverse effects in adults; however, there is greater uncertainty about the effects of larger doses, which may cause hypercalcaemia in some people [SACN, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
  - However, the SACN report identified three studies that reported adverse effects with lower doses of vitamin D:
    - One randomized controlled trial (RCT) [Sanders et al, 2010 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))] of women in Australia (n = 2256 women aged 70 years and older) reported an increased risk of fracture in the vitamin D<sub>3</sub> supplemented group (single annual dose of 12,500 micrograms/500,000 IU for 3–5 years) compared with the placebo group (incident ratio rate [IRR] = 1.15; 95% CI, 1.02–1.30 for fractures; IRR, 1.26; 95% CI, 1.00–1.59 for falls).
    - A second RCT [Bischoff-Ferrari et al, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))] of community-dwelling adults (n = 200 adults aged 70 years and older with a prior fall) randomized to receive a monthly dose of either 600 micrograms (24,000 IU) vitamin D<sub>3</sub>, 1500 micrograms (60,000 IU) vitamin D<sub>3</sub>, or 600 micrograms (24,000 IU) vitamin D<sub>3</sub> plus 300 micrograms of 25(OH)D<sub>3</sub> for 12 months reported that the incidence of falls was significantly higher in the 1500 micrograms (60,000 IU) vitamin D<sub>3</sub> group (66.9%; 95% CI, 54.4–77.5%) and the 600 micrograms (24,000 IU) vitamin D<sub>3</sub> plus 300 microgram 25(OH)D<sub>3</sub> group (66.1%; 95% CI, 53.5–76.8%) compared with the 600 microgram (24,000 IU) vitamin D<sub>3</sub> group (47.9%; 95% CI, 35.8–60.3%) (p = 0.048).
    - Another study [Smith et al, 2007 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))] reported a significant increase in non-vertebral fracture in women (but not men) given an annual intra-muscular injection of vitamin D<sub>2</sub> (7500 micrograms/300,000 IU). No effect was observed on the frequency of falls.

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What lifestyle advice should I give a person with vitamin D deficiency?

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#### Give information and advice on:

- **Safe sun exposure.** Advise that:
  - Exposing commonly uncovered areas of the skin (such as the forearms and hands) for short periods when in strong sunlight provides vitamin D. Longer periods of exposure may be needed for those with darker skin.
    - Many people will have experienced sunburn. They can use this experience to know what their skin looks like normally, how it reacts to sunlight, how long they can be exposed without risking sunburn, and how to protect their skin accordingly.
    - Advise that skin that is not usually exposed to sunlight (for example the back, abdomen and shoulders) is particularly likely to burn, so extra care is needed.
  - Prolonged exposure to strong sunlight (for example leading to burning or tanning) does not lead to excess production of vitamin D, as a regulation mechanism exists to destroy excess vitamin D, but increases the risk of skin cancer.
  - Between March and October in the UK, people should protect their skin from burning by covering up with suitable clothing (such as long-sleeved tops, a broad-brimmed hat, or long skirts and trousers); seeking shade (especially between 11am and 3pm); and applying sunscreen, which should:
    - Meet minimum standards for ultraviolet A (UVA) protection – the label should have the letters 'UVA' in a circle logo and should preferably state that it provides good UVA protection (for example at least '4-star UVA protection').
    - Provide at least sun protection factor (SPF) 15 to protect against UVB.

- Be applied liberally and frequently, according to the manufacturer's instructions. If the sunscreen is applied too thinly, the amount of protection it gives is reduced.
- Sunbeds are not an effective method of protecting against vitamin D deficiency because they emit high levels of UVA, which do not contribute to vitamin D synthesis but increase the risk of skin cancer.
- **Dietary intake of vitamin D.** Advise that:
  - It is important to maintain dietary intake of vitamin D by taking vitamin D supplements, especially during the winter months, as it is difficult to obtain sufficient vitamin D from food sources alone because they are limited.
  - Rich sources include cod liver oil (this also contains vitamin A which can be harmful in high doses and should be avoided in pregnancy), oily fish (such as salmon, mackerel, and sardines). Egg yolk, meat, offal, milk, mushrooms, and fortified foods (such as fat spreads and some breakfast cereals and yoghurts) contain small amounts.
- **Dietary intake of calcium.** Advise that:
  - It is also important to maintain dietary intake of calcium, as both calcium and vitamin D are needed to prevent long-term adverse effects on the bones.
  - Rich sources of calcium include dairy foods (milk, cheese, and yoghurts) and tinned sardines with bones.
- **Adherence to long-term supplementation.**
  - Explain that long-term supplementation with vitamin D and, where necessary, calcium should be adhered to in order to prevent recurrence of deficiency and to maintain bone health.
- **Sources of additional information.**
  - The British Dietetic Association has useful factsheets on [Vitamin D](https://www.bda.uk.com/foodfacts/VitaminD.pdf) (<https://www.bda.uk.com/foodfacts/VitaminD.pdf>) and [Calcium](https://www.bda.uk.com/foodfacts/Calcium.pdf) (<https://www.bda.uk.com/foodfacts/Calcium.pdf>) (available at [www.bda.uk.com](https://www.bda.uk.com/) (<https://www.bda.uk.com/>)).
  - The NHS choices website has a useful publication on [Vitamins and minerals - Vitamin D](http://www.nhs.uk/Conditions/vitamins-minerals/Pages/Vitamin-D.aspx) (<http://www.nhs.uk/Conditions/vitamins-minerals/Pages/Vitamin-D.aspx>) (available at [www.nhs.uk](http://www.nhs.uk/) (<http://www.nhs.uk/pages/home.aspx>)).
  - The Met Office ([www.metoffice.gov.uk](http://www.metoffice.gov.uk/) (<http://www.metoffice.gov.uk/>)) provides information on the UV index, which is an indicator of the sun's strength for a given location, date and time. This information, combined with skin type and behaviour, can be used to assess someone's risk of sunburn.

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## Basis for recommendation

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These recommendations are largely based on expert opinion in the National Institute for Health and Care Excellence (NICE) guidelines *Sunlight exposure: risks and benefits* [NICE, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))] and *Vitamin D: increasing supplement use in at-risk groups* [NICE, 2014 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))], the Scientific Advisory Committee on Nutrition (SACN) guideline *Vitamin D and health* [SACN, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))], and the Consensus Vitamin D position statement (which represents the unified views of the British Association of Dermatologists, Cancer Research UK, Diabetes UK, the Multiple Sclerosis Society, the National Heart Forum, the National Osteoporosis Society and the Primary Care Dermatology Society) [BAD et al, 2010 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].

- NICE does not describe the exact amount of sunlight exposure sufficient to stimulate cutaneous vitamin D production, but states that 'exposing commonly uncovered areas of skin, such as forearms and hands, for short periods when in strong sunlight provides vitamin D. (Longer periods of exposure may be needed for those with darker skin.)' [NICE, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]. This is in line with recommendation in the SACN report and the Consensus Vitamin D position statement.
  - SACN were unable to make any recommendations regarding the amount of sunlight exposure that would be needed during the summer months to maintain serum 25-hydroxyvitamin D (25[OH]D) levels of 25 nmol/L or greater during the winter months, as environmental and personal factors greatly affect cutaneous vitamin D production [SACN, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
  - Expert opinion in the consensus position statement is that [BAD et al, 2010 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]:
    - It is impractical to offer a one-size-fits-all recommendation for the amount of sun exposure that people need to make sufficient vitamin D, as this varies according to a number of factors (environmental, physical, and personal).
    - The time needed to make sufficient vitamin D is typically short and less than the amount of time needed for skin to redden and burn. Regularly going outside for a matter of minutes around midday without sunscreen should be enough.
    - When it comes to sun exposure, little and often is best, and the more skin that is exposed, the greater the chance of making enough vitamin D before burning.
    - People should get to know their own skin to understand how long they can spend outside before risking sunburn.
- Expert opinion in the British Medical Journal (BMJ) Best Practice review article *Vitamin D deficiency* is that usually, exposure of the arms and legs (with sun protection on the face) for about 5 to 30 minutes (depending on degree of skin pigmentation, time of day, season, latitude, and age of the person) between 10 am and 3 pm twice a week is sufficient for vitamin D synthesis [BMJ, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].

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## How should I follow up a person on high-dose vitamin D treatment?

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- **Within one month of completing high-dose vitamin D treatment**, check adjusted serum calcium levels. Consider checking serum calcium levels more regularly (for example every 1–2 weeks in the first months of treatment) in people receiving calcium supplements in addition to high-dose vitamin D treatment.
  - **If hypercalcaemia is identified:**
    - Assess the person's state of hydration, and consider admission if the person is dehydrated.
    - If the person is taking calcium supplements, advise them to stop taking them.

- If calcium levels are normal:
  - Do not recommend long-term calcium supplements.
  - If the person is taking calcium supplements, advise them to stop taking them.
- If hypocalcaemia is identified:
  - Advise the use of an over-the-counter calcium supplement containing 1–2 g of calcium. This may be needed long term (in addition to vitamin D maintenance treatment) for people with [inadequate dietary calcium intake \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!scenarioRecommendation:1\)](#).
  - If the person is already taking a calcium supplement, refer to secondary care.
- After 3–6 months of treatment with high-dose vitamin D, check serum 25-hydroxyvitamin D (25[OH]D) levels.
  - If serum 25(OH)D levels are below 50 nmol/L, refer to secondary care for consideration of possible causes, including poor compliance with treatment, [drug interactions \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!prescribingInfoSub:4\)](#), or an [underlying disease \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!backgroundSub:1\)](#), such as renal disease, liver disease, or malabsorption.
  - If serum 25(OH)D levels are greater than 50 nmol/L and there are no [signs \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!prescribingInfoSub:3\)](#) of hypercalcaemia:
    - Prescribe a daily maintenance dose of 800 international units (IU). (Higher doses of up to 2000 IU a day, occasionally up to 4000 IU a day, may be used for certain groups of people, for example those with malabsorption disorders.)
    - Reinforce [lifestyle advice \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!scenarioRecommendation:2\)](#) to prevent recurrence.
  - If symptoms and signs have not improved despite satisfactory 25(OH)D levels, consider an [alternative diagnosis \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!diagnosisSub:2\)](#).

Basis for recommendation

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### Checking adjusted serum calcium levels

- The National Osteoporosis Society (NOS) guideline *Vitamin D and bone health: a practical clinical guideline for patient management* recommends checking adjusted serum calcium levels within 1 month of completing the loading regimen, in case primary hyperparathyroidism has been unmasked [[National Osteoporosis Society, 2013 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].
- Expert opinion in the British National Formulary (BNF) [[BNF 72, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)] and in local vitamin D guidelines [[Hull and Anastasiadis, 2011 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#); [Camden Clinical Commissioning Group NHS, 2014 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#); [NHS Wales, 2014 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)] is that serum calcium levels should be checked more regularly in people who are also receiving calcium supplements, to determine how long calcium supplementation is needed and to reduce the risk of hypercalcaemia.
  - One expert reviewer of this CKS topic suggests that there is good evidence to support this recommendation but recognised that this more regular blood testing does not happen in clinical practice. CKS therefore recommends considering the need for more regular checks in this group of people.

### Checking serum hydroxyvitamin D (25[OH]D) levels

- Based on evidence suggesting that a new steady state 25(OH)D level is reached after about 3 months of vitamin D treatment (6 months in another study), NOS recommends that a minimum of 3 months treatment must be given before checking 25(OH)D levels and that it may be more prudent to wait until after 6 months have passed [[National Osteoporosis Society, 2013 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].
- The recommendation to refer people who have not responded to vitamin D treatment is based on expert opinion in the BNF [[BNF 72, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)] and is in line with recommendations in the NOS guideline *Vitamin D and bone health: a practical clinical guideline for management in children and young people* [[National Osteoporosis Society, 2015 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].

### Daily maintenance dose

- Following treatment for vitamin D deficiency, people will generally need lifelong preventative vitamin D treatment, as lifestyle changes may not be effective enough to maintain optimum vitamin D levels [[Pearce et al, 2011 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)]. In addition, people who are unable to take sufficient dietary calcium will require long-term calcium supplements [[NHS Wales, 2014 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#); [NHS Wales, 2014 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#); [BNF 72, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].
- The NOS guideline *Vitamin D and bone health: a practical clinical guideline for patient management* states that maintenance doses may be considered after high-dose vitamin D treatment, with doses equivalent to 800–2000 international units (IU) daily (occasionally up to 4000 IU daily) [[National Osteoporosis Society, 2013 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)]. An expert opinion of a reviewer of this CKS topic is that 800 IU a day is sufficient for most people, except people with malabsorption syndromes.
- The recommendation on when to consider an alternative diagnosis is extrapolated from the NOS vitamin D guideline for children and young people [[National Osteoporosis Society, 2015 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)].

## Scenario: Prevention of vitamin D deficiency in adults

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From age 18 years onwards.

How can I prevent vitamin D deficiency in adults?

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To prevent vitamin D deficiency:

- Advise that all adults living in the UK, including people at [increased risk](#) ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!backgroundSub:2](#)) of vitamin D deficiency, should take a daily supplement containing 400 international units (IU [10 micrograms]) of vitamin D throughout the year, including in the winter months.
  - Advise that:
    - Pregnant and breastfeeding women eligible for the NHS [Healthy Start](#) (<https://www.healthystart.nhs.uk/healthy-start-vouchers/do-i-qualify/>) scheme (<https://www.healthystart.nhs.uk/healthy-start-vouchers/do-i-qualify/>) can obtain free vitamin tablets by taking their coupons to a local distribution point. The daily dose of one tablet contains 400 IU of vitamin D, 400 micrograms of folic acid, and 70 mg of vitamin C. The Healthy Start vitamin tablets are suitable for vegetarians; free from wheat, fish, egg, and salt; and have no colours, flavours, preservatives, or gluten-containing ingredients.
    - All other people can purchase multivitamin preparations (tablets, capsules, and liquids) containing 400 IU of vitamin D from pharmacies. Allergies and dietary restrictions should be considered before buying these preparations to ensure that their content is safe and appropriate.
  - Do not routinely monitor serum vitamin D levels.
- Calculate dietary calcium intake.
  - Several online calcium calculators are available, such as the [Institute of Genetics and Molecular Medicine calcium calculator](#) (<http://www.cgem.ed.ac.uk/research/rheumatological/calcium-calculator>).
  - If dietary calcium intake is less than 700 mg a day, advise on dietary measures to correct this.
    - See the British Dietetic Association (BDA) factsheet on [Calcium](#) (<https://www.bda.uk.com/foodfacts/Calcium.pdf>) (available at [www.bda.uk.com](http://www.bda.uk.com/) (<https://www.bda.uk.com/>)) for information on how the recommended daily calcium intake can be achieved.
  - For people who are unable or unwilling to increase dietary calcium, consider the need for calcium supplementation.
    - Combined calcium and vitamin D preparations (such as CalciChew D3®) are available; however, the unpalatability of the calcium component may reduce compliance. Over-the-counter multivitamins provide an adequate amount of calcium (1–2 g) and vitamin D (400 IU), may be more palatable, and are a cost-effective option for people who are not exempt from prescription charges.
    - If a combined vitamin D and calcium preparation is indicated and appropriate, see the [British National Formulary](#) (<https://www.evidence.nhs.uk/formulary/bnf/current>) (BNF) for a list of available products and their recommended doses.
  - Check serum calcium levels 1 month after starting calcium supplements (and as clinically indicated thereafter).
    - If hypercalcaemia is detected, stop the calcium supplement and investigate the cause of hypercalcaemia.
- Give [lifestyle advice](#) ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!scenarioRecommendation:5](#)) to reduce the risk of vitamin D deficiency.

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Basis for recommendation

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## Vitamin D supplements for all adults in the UK

- This recommendation is based on the Scientific Advisory Committee on Nutrition (SACN) report on *Vitamin D and health* [SACN, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]. The basis for the SACN recommendations has been briefly summarized in this section. For detailed information on the evidence SACN used to develop these recommendations, see the [full SACN report](#) ([https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/537616/SACN\\_Vitamin\\_D\\_and\\_Health\\_report.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/537616/SACN_Vitamin_D_and_Health_report.pdf)) (available at [www.gov.uk](http://www.gov.uk/) (<http://www.gov.uk/>)).
  - SACN reviewed the evidence on a number of health outcomes associated with vitamin D to assess whether any might be used to inform the setting of Dietary Reference Values (DRVs) for vitamin D.
  - There was insufficient evidence from non-musculoskeletal health outcomes (including reproductive health [on maternal and newborn outcomes], cancers, cardiovascular disease, hypertension, all-cause mortality, immune modulation, infectious diseases, neuropsychological functioning, age-related macular degeneration, and oral health) to inform the setting of DRVs. However, the evidence on musculoskeletal health outcomes (osteomalacia, falls, and muscle strength and function) was considered to be suggestive of a beneficial effect of vitamin D and was therefore used as the basis for setting the DRVs.
  - Based on the evidence for musculoskeletal outcomes, which showed an increase risk of poor musculoskeletal health at serum hydroxyvitamin D (25[OH]D) concentrations less than 25 nmol/L, SACN recommends a vitamin D reference nutrient intake (RNI) of 400 international units (IU [10 micrograms]) daily for all adults in the UK, including those at increased risk of vitamin D deficiency.
  - An increment to the RNI was not considered necessary for people at increased risk of vitamin D deficiency because the recommendation for the RNI to be applicable throughout the year is to take account of people with minimal sunshine exposure, including those most at risk.
  - According to the SACN report:
    - These recommendations are a precautionary approach to protect the most vulnerable groups in the population, take account of variable exposure to sunshine and diet, and ensure coverage of 97.5% of the population throughout the year. Although most people would be expected to synthesise vitamin D during the summer months, serum 25(OH)D concentrations below 25 nmol/L have been observed in a proportion of some population groups in the UK during the summer months. Since it is not possible to identify these people, the recommendation is applicable to the UK population throughout the year.
    - Although achievement of the proposed RNI by the UK population would lead to an increase in mean/median vitamin D intakes of the UK population, it is unlikely that this would lead to vitamin D intakes at the upper end of the distribution reaching levels that might pose a risk of adverse effects.

## Not routinely monitoring serum vitamin D levels

- This recommendation is extrapolated from the SACN vitamin D report [SACN, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))] and the National Osteoporosis Society (NOS) guideline *Vitamin D and bone health: a practical clinical guide for patient management* [National Osteoporosis Society, 2013 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].

- SACN does not recommend routine monitoring of serum vitamin D levels during long-term supplementation with vitamin D.
- Expert opinion in the NOS guideline is that routine monitoring of serum 25(OH)D levels is unnecessary for people on long-term maintenance doses of vitamin D (up to 2000 IU a day).

## Ensuring adequate calcium intake

- Adequate levels of both vitamin D and dietary calcium are needed to ensure optimum serum calcium levels, and it is important to ensure that both are maintained to prevent long-term adverse effects on the bones [DTB, 2006 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#)); Kennel et al, 2010 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#)); BMJ, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]. People who are unable to take sufficient dietary calcium will therefore require long-term calcium supplements [NHS Wales, 2014 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#)); BNF 72, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
- The recommendation to consider the need for supplemental calcium only when an adequate dietary intake of calcium cannot be achieved is extrapolated from expert opinion in the National Osteoporosis Guideline Group (NOGG) guideline *Osteoporosis: clinical guideline for prevention and treatment*, which states that it may be prudent to increase dietary calcium intake and use vitamin D alone where the use of calcium and vitamin D supplementation might otherwise be considered. In their expert opinion [NOGG, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]:
  - Compliance and persistence with calcium-containing supplements is poor (possibly due to the unpalatability of the calcium component).
  - High dietary calcium does not seem to carry the same increased risk of cardiovascular events as has been suggested for calcium supplements in several studies (although these studies have been widely criticized and the putative association requires further clarification).
- The recommended dose of calcium (1–2 g) is in line with the Institute of Medicine (IOM)'s recommended dietary calcium allowance for adults aged 18 years and older [IOM, 2010 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
- NOS recommends checking adjusted serum calcium levels 1 month after starting vitamin D supplementation in case primary hyperparathyroidism has been unmasked [National Osteoporosis Society, 2013 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
- The recommendation on how to manage hypercalcaemia is based on what CKS considers to be good clinical practice.

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What lifestyle advice should I give to reduce the risk of vitamin D deficiency?

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## Give information and advice on:

- **Safe sun exposure.** Advise that:
  - Exposing commonly uncovered areas of the skin (such as the forearms and hands) for short periods when in strong sunlight provides vitamin D. (Longer periods of exposure may be needed for those with darker skin.)
    - Many people will have experienced sunburn. They can use this experience to know what their skin looks like normally, how it reacts to sunlight, how long they can be exposed without risking sunburn, and how to protect their skin accordingly.
    - Advise that skin that is not usually exposed to sunlight (for example the back, abdomen and shoulders) is particularly likely to burn, so extra care is needed.
  - Prolonged exposure to strong sunlight (for example leading to burning or tanning) does not lead to excess production of vitamin D, as a regulation mechanism exists to destroy excess vitamin D, but increases the risk of skin cancer.
  - Between March and October in the UK, people should protect their skin from burning by covering up with suitable clothing (such as long-sleeved tops, a broad-brimmed hat, or long skirts and trousers); seeking shade (especially between 11am and 3pm); and applying sunscreen, which should:
    - Meet minimum standards for ultraviolet A (UVA) protection – the label should have the letters 'UVA' in a circle logo and should preferably state that it provides good UVA protection (for example at least '4-star UVA protection').
    - Provide at least sun protection factor (SPF) 15 to protect against UVB.
    - Be applied liberally and frequently, according to the manufacturer's instructions. If the sunscreen is applied too thinly, the amount of protection it gives is reduced.
  - Sunbeds are not an effective method of protecting against vitamin D deficiency because they emit high levels of UVA, which do not contribute to vitamin D synthesis but increase the risk of skin cancer.
- **Dietary intake of vitamin D.** Advise that:
  - It is important to maintain dietary intake of vitamin D by taking vitamin D supplements, especially during the winter months, as it is difficult to obtain sufficient vitamin D from food sources alone because they are limited.
  - Rich sources include cod liver oil (this also contains vitamin A which can be harmful in high doses and should be avoided in pregnancy), oily fish (such as salmon, mackerel, and sardines). Egg yolk, meat, offal, milk, mushrooms, and fortified foods (such as fat spreads and some breakfast cereals and yoghurts) contain small amounts.
- **Dietary intake of calcium.** Advise that:
  - It is also important to maintain dietary intake of calcium, as both calcium and vitamin D are needed to prevent long-term adverse effects on the bones.
  - Rich sources of calcium include dairy foods (milk, cheese, and yoghurts) and tinned sardines with bones.
- **Adherence to long-term supplementation.**
  - Explain that long-term supplementation with vitamin D and, where necessary, calcium should be adhered to in order to prevent recurrence of deficiency and to maintain bone health.
- **Sources of additional information.**
  - The British Dietetic Association has useful factsheets on [Vitamin D](#) (<https://www.bda.uk.com/foodfacts/VitaminD.pdf>) and [Calcium](#) (<https://www.bda.uk.com/foodfacts/Calcium.pdf>) (available at [www.bda.uk.com](https://www.bda.uk.com/) (<https://www.bda.uk.com/>)).
  - The NHS choices website has a useful publication on [Vitamins and minerals - Vitamin D](#) (<http://www.nhs.uk/Conditions/vitamins-minerals/Pages/Vitamin-D.aspx>) (available at [www.nhs.uk](http://www.nhs.uk) (<http://www.nhs.uk/pages/home.aspx>)).

- The Met Office ([www.metoffice.gov.uk](http://www.metoffice.gov.uk) (<http://www.metoffice.gov.uk/>)) provides information on the UV index, which is an indicator of the sun's strength for a given location, date and time. This information, combined with skin type and behaviour, can be used to assess someone's risk of sunburn.

## Basis for recommendation

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These recommendations are largely based on expert opinion in the National Institute for Health and Care Excellence (NICE) guidelines *Sunlight exposure: risks and benefits* [NICE, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))] and *Vitamin D: increasing supplement use in at-risk groups* [NICE, 2014 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))], the Scientific Advisory Committee on Nutrition (SACN) guideline *Vitamin D and health* [SACN, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))], and the Consensus Vitamin D position statement (which represents the unified views of the British Association of Dermatologists, Cancer Research UK, Diabetes UK, the Multiple Sclerosis Society, the National Heart Forum, the National Osteoporosis Society and the Primary Care Dermatology Society) [BAD et al, 2010 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].

- NICE does not describe the exact amount of sunlight exposure sufficient to stimulate cutaneous vitamin D production, but states that 'exposing commonly uncovered areas of skin, such as forearms and hands, for short periods when in strong sunlight provides vitamin D. (Longer periods of exposure may be needed for those with darker skin.)' [NICE, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]. This is in line with recommendation in the SACN report and the Consensus Vitamin D position statement.
- SACN were unable to make any recommendations regarding the amount of sunlight exposure that would be needed during the summer months to maintain serum 25-hydroxyvitamin D (25[OH]D) levels of 25 nmol/L or greater during the winter months, as environmental and personal factors greatly affect cutaneous vitamin D production [SACN, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
- Expert opinion in the consensus position statement is that [BAD et al, 2010 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]:
  - It is impractical to offer a one-size-fits-all recommendation for the amount of sun exposure that people need to make sufficient vitamin D, as this varies according to a number of factors (environmental, physical, and personal).
  - The time needed to make sufficient vitamin D is typically short and less than the amount of time needed for skin to redden and burn. Regularly going outside for a matter of minutes around midday without sunscreen should be enough.
  - When it comes to sun exposure, little and often is best, and the more skin that is exposed, the greater the chance of making enough vitamin D before burning.
  - People should get to know their own skin to understand how long they can spend outside before risking sunburn.
- Expert opinion in the British Medical Journal (BMJ) Best Practice review article *Vitamin D deficiency* is that usually, exposure of the arms and legs (with sun protection on the face) for about 5 to 30 minutes (depending on degree of skin pigmentation, time of day, season, latitude, and age of the person) between 10 am and 3 pm twice a week is sufficient for vitamin D synthesis [BMJ, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].

## High-dose vitamin D

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What vitamin D preparations are available to treat vitamin D deficiency or insufficiency?

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- For the treatment of vitamin D deficiency, there are several high-dose vitamin D preparations available. However, most do not have a UK license.
  - The British National Formulary (BNF) lists the preparations below [BNF 72, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]:
    - Ergocalciferol (vitamin D<sub>2</sub>) non-proprietary tablets — available in 250 micrograms (10,000 international units [IU] and 1.25 mg (50,000 IU) tablets.
    - Ergocalciferol capsules — available in 1.25 mg (50,000 IU) [ABPI, 2016a ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].
    - Ergocalciferol intramuscular injection containing 7.5 mg (300,000 IU) of vitamin D<sub>2</sub> per mL —available in 1 and 2 mL ampoules.
    - Fultium-D3® (colecalciferol) capsules — available in 80 micrograms (3200 IU) and 500 micrograms (20,000 IU) capsules.
    - InVita D3® (colecalciferol) oral solution — available in 625 micrograms (25,000 IU) per mL ampoules.
  - Detailed information on these products is available in the BNF ([www.evidence.nhs.uk](http://www.evidence.nhs.uk) (<http://www.evidence.nhs.uk/>)) and the manufacturers' Summaries of Product Characteristics (SPCs, [www.medicines.org.uk](http://www.medicines.org.uk) (<http://www.medicines.org.uk/emc/>)).
- For the treatment of vitamin D deficiency:
  - The BNF lists the following preparations [BNF 72, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]:
    - Fultium-D3® (colecalciferol) 20 micrograms (800 IU) capsules.
    - Desunin® (colecalciferol) tablets — available in 20 micrograms (800 IU) and 100 micrograms (4,000 IU).
  - There are no products containing maintenance doses of ergocalciferol alone.
- Unlicensed formulations of vitamin D preparations are available from 'special-order' manufacturers and specialist importing companies.
  - The East and South East England Specialist Pharmacy Services document [Vitamin D deficiency and Insufficiency: using appropriate available products](https://www.sps.nhs.uk/wp-content/uploads/2014/08/fileMDs3Nzg2ODU7L3VwbG9hZC9kb2N1bWVudHMvQ29tbXVuaXRpZXMvU1BTX0VfU0VfRW5nbGFuZC9WaXRhbWlue) (<https://www.sps.nhs.uk/wp-content/uploads/2014/08/fileMDs3Nzg2ODU7L3VwbG9hZC9kb2N1bWVudHMvQ29tbXVuaXRpZXMvU1BTX0VfU0VfRW5nbGFuZC9WaXRhbWlue>) has a comprehensive (but not exhaustive) list of available vitamin D products, including unlicensed products.
- For people with peanut or soya allergy, see the UK Medicines Information (UKMi) document [Is there a suitable vitamin D product for a patient with a peanut or soya allergy?](https://www.sps.nhs.uk/articles/is-there-a-suitable-vitamin-d-product-for-a-patient-with-a-peanut-or-soya-allergy/) (<https://www.sps.nhs.uk/articles/is-there-a-suitable-vitamin-d-product-for-a-patient-with-a-peanut-or-soya-allergy/>), available on the NICE Evidence website ([www.evidence.nhs.uk](http://www.evidence.nhs.uk/search?q=%22Is+there+a+suitable+vitamin+D+product+for+a+patient+with+a+peanut+or+soya+allergy%22) (<http://www.evidence.nhs.uk/search?q=%22Is+there+a+suitable+vitamin+D+product+for+a+patient+with+a+peanut+or+soya+allergy%22>)), for information on suitable peanut and soya-free vitamin D preparations.
- For people on a vegetarian or vegan diet, see the UKMi document [Which vitamin D preparations are suitable for a vegetarian or vegan diet?](https://www.sps.nhs.uk/articles/which-vitamin-d-preparations-are-suitable-for-a-vegetarian-or-vegan-diet/) (<https://www.sps.nhs.uk/articles/which-vitamin-d-preparations-are-suitable-for-a-vegetarian-or-vegan-diet/>) for information on suitable preparations.

- For people with halal or kosher requirements, the UKMi document [Which vitamin D preparations are suitable for a vegetarian or vegan diet?](https://www.sps.nhs.uk/articles/which-vitamin-d-preparations-are-suitable-for-a-vegetarian-or-vegan-diet/) (<https://www.sps.nhs.uk/articles/which-vitamin-d-preparations-are-suitable-for-a-vegetarian-or-vegan-diet/>) has some information on halal and kosher compliant vitamin D products.

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## What are the contraindications and cautions for vitamin D?

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- Do not prescribe vitamin D preparations to people with:
  - Hypercalcaemia or hypercalciuria (or diseases or conditions which can cause these problems).
  - Metastatic calcification.
  - Hypervitaminosis D.
  - Nephrolithiasis.
  - Severe renal impairment — vitamin D<sub>3</sub> and D<sub>2</sub> are not metabolized normally; other forms of vitamin D should be used.
- Prescribe vitamin D with caution to:
  - People with mild to moderate renal impairment.
  - People with a co-existing condition associated with increased sensitivity to vitamin D (such as sarcoidosis, tuberculosis, lymphoma, or primary hyperparathyroidism) — consider seeking specialist advice.
  - Pregnant women — consider seeking specialist advice.
  - Breastfeeding women (due to the risk of hypercalcaemia in the infant).
  - People taking [certain drugs](#) ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!prescribingInfoSub:4](#)).

[[ABPI, 2015](#) ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#)); [BNF 72, 2016](#) ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]

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## What are the adverse effects of vitamin D?

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- Vitamin D toxicity (which rarely occurs unless the vitamin D dose is very high) manifests mainly through chronic hypercalcaemia, leading to deposition of calcium in soft tissues, diffuse mineralization of bone, and irreversible renal and cardiovascular toxicity.
  - The clinical features of hypercalcaemia include:
    - Nausea and vomiting.
    - Diarrhoea.
    - Constipation.
    - Anorexia and weight loss.
    - Lethargy.
    - Polyuria and thirst.
    - Sweating.
    - Headache.
    - Vertigo.
    - Raised concentrations of calcium and phosphate in plasma and urine.
- If hypercalcaemia is suspected, check serum calcium levels. If hypercalcaemia is identified:
  - Assess the person's state of hydration, and consider admission if the person is dehydrated.
  - If the person is taking a calcium supplement, advise that it should be stopped.
- Other adverse effects that have been linked with high vitamin D intakes or high serum 25-hydroxyvitamin D (25 [OH]D) concentrations include an increased incidence of falls and fractures, an increased rates of pancreatic and prostate cancer, and increased total mortality (that is, from all causes combined). However, evidence for these associations is less robust and consistent than that relating to hypercalcaemia [[SACN, 2016](#) ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].

[[BNF 72, 2016](#) ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#)); [SACN, 2016](#) ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]

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## What drug interactions are associated with vitamin D?

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- The key drug interactions associated with vitamin D are listed below. Seek specialist advice as appropriate during concurrent treatment with these drugs.
  - Antiepileptic drugs (phenytoin or barbiturates) — can increase the metabolism of vitamin D, leading to a reduction in the effects of vitamin D.
    - Higher doses of vitamin D may be needed.
  - Cardiac glycosides — excessive dosing of vitamin D can induce hypercalcaemia, which may enhance the effects of digoxin and other cardiac glycosides (leading to an increased risk of digoxin toxicity and serious arrhythmias).
    - Close monitoring (and possibly a dose reduction of vitamin D) is needed during concurrent use.
  - Corticosteroids — may increase vitamin D metabolism and elimination.
    - Higher doses of vitamin D may be needed.
  - Ion exchange resins (such as colestyramine) or laxatives (such as paraffin oil) — may reduce the gastrointestinal absorption of vitamin D.
    - Higher doses of vitamin D may be needed.



- Miconazole — the effects of vitamin D are possibly reduced by miconazole.
  - Higher doses of vitamin D may be needed.
- Orlistat — may prevent the absorption of vitamin D, even in people also taking multivitamins.
  - Advise that vitamin D preparations should be taken at least 2 hours after taking orlistat. It may be necessary to monitor vitamin D levels, even if multivitamins are given [Preston, 2015 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references)].
- Thiazide diuretics (such as bendroflumethiazide) — may reduce the urinary excretion of calcium thereby increasing the risk of hypercalcaemia.
  - Close monitoring (and possibly a dose reduction of vitamin D) is needed during concurrent use.

[ABPI, 2015 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references); BNF 72, 2016 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references)]

## Calcium supplements

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Which calcium preparations are available?

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- There are several calcium preparations listed in the British National Formulary (BNF).
  - Examples include [BNF 72, 2016 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references)]:
    - Adcal® fruit flavoured tablets (containing calcium carbonate 1.5 g [calcium 600 mg or 15 mmol]).
    - Cacit® effervescent tablets (containing calcium carbonate 1.25 g, providing calcium citrate when dispersed in water [calcium 500 mg or 12.5 mmol]).
    - Sandocal® 1000 effervescent tablets (containing calcium lactate gluconate 2.263 g and calcium carbonate 1.75 g, [calcium 1 g or 25 mmol]).
  - See the BNF ([www.evidence.nhs.uk](http://www.evidence.nhs.uk) (<http://www.evidence.nhs.uk/>)) for a list of available products.
- Multivitamin preparations (tablets, capsules, and liquids) containing calcium are also available to buy from pharmacies.

What are the contraindications and cautions for calcium supplements?

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- Do not prescribe calcium supplements to people with:
  - Severe hypercalcaemia and/or hypercalciuria (for example in hyperparathyroidism, vitamin D overdose, and decalcifying tumours [such as plasmacytoma and skeletal metastases]).
  - Severe renal failure untreated by renal dialysis.
  - Osteoporosis due to immobilization.
  - Nephrolithiasis.
- Prescribe calcium supplements with caution to people with:
  - Mild to moderate renal impairment.
  - A co-existing condition associated with increased sensitivity to vitamin D (such as sarcoidosis, tuberculosis, lymphoma, or primary hyperparathyroidism) — consider seeking specialist advice.
  - A history of nephrolithiasis.
  - Respiratory acidosis or respiratory failure.

[ABPI, 2016b (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references); BNF 72, 2016 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references)]

What are the adverse effects of calcium supplements?

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- Adverse effects of calcium supplements are uncommon.
- Overdose can lead to hypercalcaemia, hypercalciuria, and, very rarely, milk-alkali syndrome (characterized by frequent urge to urinate; continuing headache; continuing loss of appetite; nausea or vomiting; unusual tiredness or weakness; hypercalcaemia, alkalosis, and renal impairment).
- Rarely, gastrointestinal adverse effects (such as constipation, dyspepsia, flatulence, nausea, abdominal pain, and diarrhoea) may occur.
- Very rarely, skin disorders (such as itching, rash, and urticaria) may occur.

[ABPI, 2016b (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references); BNF 72, 2016 (/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references)]

What drug interactions are associated with calcium supplements?

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- The key drug interactions associated with calcium are listed below. Seek specialist advice as appropriate during concurrent treatment with these drugs.
  - Bisphosphonate — calcium salts reduce absorption of bisphosphonates.
    - Bisphosphonate should be taken at least three hours before taking calcium supplements.
  - Cardiac glycosides — calcium supplements can induce hypercalcaemia, which may enhance the effects of digoxin and other cardiac glycosides (leading to an increased risk of digitalis toxicity and serious arrhythmias).
    - Close monitoring is needed during concurrent use.

- **Systemic corticosteroids** — absorption of calcium salts may be reduced by corticosteroids.
  - It may be necessary to increase the dose of the calcium supplement.
- **Thiazide diuretics** — may reduce the urinary excretion of calcium thereby increasing the risk of hypercalcaemia.
  - Close monitoring (and possibly a dose reduction of calcium) is needed during concurrent use.
- **Tetracycline antibiotics** — calcium supplements may reduce the absorption of tetracyclines.
  - Tetracyclines should be taken at least two hours before, or four to six hours after, oral intake of calcium.
- **Levothyroxine** — calcium salts reduce the absorption of levothyroxine.
  - Levothyroxine should be taken at least 4 hours before or after taking calcium salts.
- **Quinolones** — calcium salts may impair the absorption of quinolones (such as ciprofloxacin).
  - Quinolone antibiotics should be taken two hours before or after taking calcium supplements.
- **Zinc, iron, and strontium ranelate** — calcium salts reduce the absorption of zinc salts, oral iron salts, and strontium ranelate.
  - These preparations should be taken two hours before or after taking calcium supplements.

[[ABPI, 2016b \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#); [BNF 72, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)]

## Calcium and vitamin D combination products

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What do I need to know about prescribing calcium and vitamin D combination products?

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- For managing hypocalcaemia or low dietary calcium intake in people taking high-dose vitamin D:
  - Calcium-only supplements should be prescribed in addition to high-dose vitamin D, as there are no combined products containing high-dose vitamin D with calcium.
  - The available combination products contain sub-therapeutic doses of vitamin D (such as Calcichew D3<sup>®</sup>, containing 500 mg calcium and 400 units of vitamin D) and are therefore *not* recommended due to the risk of hypercalcaemia.
  - See the section on [How to treat \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!scenarioRecommendation:1\)](#) for more information.
- For managing hypocalcaemia or low dietary calcium intake in people taking maintenance doses of vitamin D:
  - Combined calcium and vitamin D preparations may be considered. However, the unpalatability of the calcium component may reduce compliance.
  - Over-the-counter multivitamins provide an adequate amount of calcium and vitamin D, may be more palatable, and are a cost-effective option for people who are not exempt from prescription charges.
  - See the section on [How to treat \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!scenarioRecommendation:1\)](#) for more information.

[[Hull and Anastasiadis, 2011 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#); [National Osteoporosis Society, 2013 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#); [Nene Clinical Commissioning Group NHS, 2016 \(/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references\)](#)]

## Search strategy

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## Scope of search

A literature search was conducted for guidelines, systematic reviews and randomized controlled trials on primary care management of vitamin D deficiency in adults.

## Search dates

Unrestricted - September 2016.

## Key search terms

Various combinations of searches were carried out. The terms listed below are the core search terms that were used for Medline.

- exp vitamin D deficiency/

## Sources of guidelines

- [National Institute for Health and Care Excellence \(NICE\) \(http://www.nice.org.uk/\)](#)
- [Scottish Intercollegiate Guidelines Network \(SIGN\) \(http://www.sign.ac.uk/\)](#)
- [Royal College of Physicians \(http://www.rcplondon.ac.uk/\)](#)
- [Royal College of General Practitioners \(http://www.rcgp.org.uk/\)](#)
- [Royal College of Nursing \(http://www.rcn.org.uk/development/practice/clinicalguidelines\)](#)
- [NICE Evidence \(https://www.evidence.nhs.uk/topics/\)](#)
- [Health Protection Agency \(http://www.hpa.org.uk/\)](#)
- [World Health Organization \(http://www.who.int/\)](#)
- [National Guidelines Clearinghouse \(http://www.guideline.gov/\)](#)
- [Guidelines International Network \(http://www.g-i-n.net/\)](#)

- [TRIP database \(http://www.tripdatabase.com/\)](http://www.tripdatabase.com/)
- [GAIN \(http://www.gain-ni.org/index.php/audits/guidelines\)](http://www.gain-ni.org/index.php/audits/guidelines)
- [NHS Scotland National Patient Pathways \(http://www.pathways.scot.nhs.uk/\)](http://www.pathways.scot.nhs.uk/)
- [New Zealand Guidelines Group \(http://www.nzgg.org.nz/\)](http://www.nzgg.org.nz/)
- [Agency for Healthcare Research and Quality \(http://www.ahrq.gov/\)](http://www.ahrq.gov/)
- [Institute for Clinical Systems Improvement \(http://www.icsi.org/\)](http://www.icsi.org/)
- [National Health and Medical Research Council \(Australia\) \(http://www.nhmrc.gov.au/publications/index.htm\)](http://www.nhmrc.gov.au/publications/index.htm)
- [Royal Australian College of General Practitioners \(http://www.racgp.org.au/your-practice/guidelines/\)](http://www.racgp.org.au/your-practice/guidelines/)
- [British Columbia Medical Association \(http://www.health.gov.bc.ca/gpac/index.html\)](http://www.health.gov.bc.ca/gpac/index.html)
- [Canadian Medical Association \(http://www.cma.ca/index.php/ci\\_id/54316/la\\_id/1.htm\)](http://www.cma.ca/index.php/ci_id/54316/la_id/1.htm)
- [Alberta Medical Association \(http://www.topalbertadoctors.org/cpgs.php\)](http://www.topalbertadoctors.org/cpgs.php)
- [University of Michigan Medical School \(http://ocpd.med.umich.edu/cme/self-study/\)](http://ocpd.med.umich.edu/cme/self-study/)
- [Michigan Quality Improvement Consortium \(http://mqic.org/guidelines.htm\)](http://mqic.org/guidelines.htm)
- [Singapore Ministry of Health \(http://www.moh.gov.sg/content/moh\\_web/home/Publications/guidelines/cpg.html\)](http://www.moh.gov.sg/content/moh_web/home/Publications/guidelines/cpg.html)
- [National Resource for Infection Control \(http://www.nric.org.uk/\)](http://www.nric.org.uk/)
- [Patient UK Guideline links \(http://www.patient.co.uk/guidelines.asp\)](http://www.patient.co.uk/guidelines.asp)
- [UK Ambulance Service Clinical Practice Guidelines \(http://www2.warwick.ac.uk/fac/med/research/hsri/emergencycare/jrcalc\\_2006/guidelines/\)](http://www2.warwick.ac.uk/fac/med/research/hsri/emergencycare/jrcalc_2006/guidelines/)
- [RefHELP NHS Lothian Referral Guidelines \(http://www.refhelp.scot.nhs.uk/index.php?option=com\\_content&task=view&id=490&Itemid=104\)](http://www.refhelp.scot.nhs.uk/index.php?option=com_content&task=view&id=490&Itemid=104)
- Medline (with guideline filter)
- [Driver and Vehicle Licensing Agency \(http://www.dft.gov.uk/dvla/medical/ata glance.aspx\)](http://www.dft.gov.uk/dvla/medical/ata glance.aspx)
- [NHS Health at Work \(http://www.nhshealthatwork.co.uk/oh-guidelines.asp\)](http://www.nhshealthatwork.co.uk/oh-guidelines.asp) (occupational health practice)

## Sources of systematic reviews and meta-analyses

- [The Cochrane Library \(http://www.thecochranelibrary.com/\)](http://www.thecochranelibrary.com/):
  - Systematic reviews
  - Protocols
  - Database of Abstracts of Reviews of Effects
- Medline (with systematic review filter)
- EMBASE (with systematic review filter)

## Sources of health technology assessments and economic appraisals

- [NIHR Health Technology Assessment programme \(http://www.hta.ac.uk/\)](http://www.hta.ac.uk/)
- [The Cochrane Library \(http://www.thecochranelibrary.com/\)](http://www.thecochranelibrary.com/):
  - NHS Economic Evaluations
  - Health Technology Assessments
- [Canadian Agency for Drugs and Technologies in Health \(http://www.cadth.ca/\)](http://www.cadth.ca/)
- [International Network of Agencies for Health Technology Assessment \(http://www.inahta.org/\)](http://www.inahta.org/)

## Sources of randomized controlled trials

- [The Cochrane Library \(http://www.thecochranelibrary.com/\)](http://www.thecochranelibrary.com/):
  - Central Register of Controlled Trials
- Medline (with randomized controlled trial filter)
- EMBASE (with randomized controlled trial filter)

## Sources of evidence based reviews and evidence summaries

- [Bandolier \(http://www.medicine.ox.ac.uk/bandolier/\)](http://www.medicine.ox.ac.uk/bandolier/)
- [Drug & Therapeutics Bulletin \(http://dtb.bmj.com/\)](http://dtb.bmj.com/)
- [TRIP database \(http://www.tripdatabase.com/\)](http://www.tripdatabase.com/)
- [Central Services Agency COMPASS Therapeutic Notes \(http://www.medicinesni.com/courses/type.asp?ID=CN\)](http://www.medicinesni.com/courses/type.asp?ID=CN)

## Sources of national policy

- [Department of Health \(http://www.dh.gov.uk/\)](http://www.dh.gov.uk/)
- Health Management Information Consortium (HMIC)

## Patient experiences

- [Healthtalkonline \(http://www.healthtalkonline.org/\)](http://www.healthtalkonline.org/)
- [BMJ - Patient Journeys \(http://www.bmj.com/bmj-series/patient-journeys\)](http://www.bmj.com/bmj-series/patient-journeys)
- [Patient.co.uk - Patient Support Groups \(http://www.patient.co.uk/selfhelp.asp\)](http://www.patient.co.uk/selfhelp.asp)

## Sources of medicines information

The following sources are used by CKS pharmacists and are not necessarily searched by CKS information specialists for all topics. Some of these resources are not freely available and require subscriptions to access content.

- [British National Formulary](http://www.evidence.nhs.uk/formulary/bnf/current) (<http://www.evidence.nhs.uk/formulary/bnf/current>)(BNF)
- [electronic Medicines Compendium](http://www.medicines.org.uk/) (<http://www.medicines.org.uk/>)(eMC)
- [European Medicines Agency](http://www.ema.europa.eu/ema/) (<http://www.ema.europa.eu/ema/>)(EMA)
- [LactMed](http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT) (<http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT>)
- [Medicines and Healthcare products Regulatory Agency](http://www.mhra.gov.uk/index.htm) (<http://www.mhra.gov.uk/index.htm>)(MHRA)
- [REPROTOX](http://www.reprotox.org/Default.aspx) (<http://www.reprotox.org/Default.aspx>)
- [Scottish Medicines Consortium](http://www.scottishmedicines.org.uk/Home) (<http://www.scottishmedicines.org.uk/Home>)
- [Stockley's Drug Interactions](https://www.medicinescomplete.com/mc/stockley/current/login.htm?uri=http%3A%2F%2Fwww.medicinescomplete.com%2Fmc%2Fstockley%2Fcurrent%2F) (<https://www.medicinescomplete.com/mc/stockley/current/login.htm?uri=http%3A%2F%2Fwww.medicinescomplete.com%2Fmc%2Fstockley%2Fcurrent%2F>)
- [TERIS](http://depts.washington.edu/terisweb/teris/) (<http://depts.washington.edu/terisweb/teris/>)
- [TOXBASE](http://www.toxbase.org/) (<http://www.toxbase.org/>)
- [Micromedex](http://www.micromedex.com/products/hcs/) (<http://www.micromedex.com/products/hcs/>)
- [UK Medicines Information](http://www.ukmi.nhs.uk/) (<http://www.ukmi.nhs.uk/>)

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## Stakeholder engagement

### Our policy

The external review process is an essential part of CKS topic development. Consultation with a wide range of stakeholders provides quality assurance of the topic in terms of:

- Clinical accuracy.
- Consistency with other providers of clinical knowledge for primary care.
- Accuracy of implementation of national guidance (in particular NICE guidelines).
- Usability.

### Principles of the consultation process

- The process is inclusive and any individual may participate.
- To participate, an individual must declare whether they have any competing interests or not. If they do not declare whether or not they have competing interests, their comments will not be considered.
- Comments received after the deadline will be considered, but they may not be acted upon before the clinical topic is issued onto the website.
- Comments are accepted in any format that is convenient to the reviewer, although an electronic format is encouraged.
- External reviewers are not paid for commenting on the draft topics.
- Discussion with an individual or an organization about the CKS response to their comments is only undertaken in exceptional circumstances (at the discretion of the Clinical Editor or Editorial Steering Group).
- All reviewers are thanked and offered a letter acknowledging their contribution for the purposes of appraisal/revalidation.
- All reviewers are invited to be acknowledged on the website. All reviewers are given the opportunity to feedback about the external review process, enabling improvements to be made where appropriate.

### Stakeholders

- Key stakeholders identified by the CKS team are invited to comment on draft CKS topics. Individuals and organizations can also register an interest to feedback on a specific topic, or topics in a particular clinical area, through the [Getting involved](http://cks.clarity.co.uk/get-involved/) (<http://cks.clarity.co.uk/get-involved/>) section of the [Clarity Informatics](https://clarity.co.uk/) (<https://clarity.co.uk/>) website.
- Stakeholders identified from the following groups are invited to review draft topics:
  - Experts in the topic area.
  - Professional organizations and societies (for example, Royal Colleges).
  - Patient organizations, Clarity has established close links with groups such as Age UK and the Alzheimer's Society specifically for their input into new topic development, review of current topic content and advice on relevant areas of expert knowledge.
  - Guideline development groups where the topic is an implementation of a guideline.
  - The British National Formulary team.
  - The editorial team that develop MeReC Publications.
- Reviewers are provided with clear instructions about what to review, what comments are particularly helpful, how to submit comments, and declaring interests.

### Patient engagement

Clarity Informatics has enlisted the support and involvement of patients and lay persons at all stages in the process of creating the content which include:

- Topic selection
- Scoping of topic
- Selection of clinical scenarios

- First draft internal review
- Second draft internal review
- External review
- Final draft and pre-publication

Our lay and patient involvement includes membership on the editorial steering group, contacting expert patient groups, organizations and individuals.

## Evidence exclusion criteria

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## Our policy

Scoping a literature search, and reviewing the evidence for CKS is a methodical and systematic process that is carried out by the lead clinical author for each topic. Relevant evidence is gathered in order that the clinical author can make fully informed decisions and recommendations. It is important to note that some evidence may be excluded for a variety of reasons. These reasons may be applied across all CKS topics or may be specific to a given topic.

Studies identified during literature searches are reviewed to identify the most appropriate information to author a CKS topic, ensuring any recommendations are based on the best evidence. We use the principles of the GRADE and PICOT approaches to assess the quality of published research. We use the principles of AGREE II to assess the quality of published guidelines.

## Standard exclusions for scoping literature:

- Animal studies
- Original research is not written in English

## Possible exclusions for reviewed literature:

- Sample size too small or study underpowered
- Bias evident or promotional literature
- Population not relevant
- Intervention/treatment not relevant
- Outcomes not relevant
- Outcomes have no clear evidence of clinical effectiveness
- Setting not relevant
- Not relevant to UK
- Incorrect study type
- Review article
- Duplicate reference

## Organizational, behavioural and financial barriers

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## Our policy

The CKS literature searches take into consideration the following concepts, which are discussed at the initial scoping of the topic.

- Feasibility
  - Studies are selected depending on whether the intervention under investigation is available in the NHS and can be practically and safely undertaken in primary care.
- Organizational and Financial Impact Analysis
- Studies are selected and evaluated on whether the intervention under investigations may have an impact on local clinical service provision or national impact on cost for the NHS. The principles of clinical budget impact analysis are adhered to, evaluated and recorded by the author. The following factors are considered when making this assessment and analysis.
  - Eligible population
  - Current interventions
  - Likely uptake of new intervention or recommendation
  - Cost of the current or new intervention mix
  - Impact on other costs
  - Condition-related costs
  - In-direct costs and service impacts
  - Time dependencies
- Cost-effectiveness or cost-benefit analysis studies are identified where available.

We also evaluate and include evidence from NICE accredited sources which provide economic evaluations of recommendations, such as NICE guidelines. When a recommended action may not be possible because of resource constraints, this is explicitly indicated to healthcare professionals by the wording of the CKS recommendation.

## Our policy

Clarity Informatics requests that all those involved in the writing and reviewing of topics, and those involved in the external review process to declare any competing interests. Signed copies are securely held by Clarity Informatics and are available on request with the permission of the individual. A copy of the declaration of interest form which participants are asked to complete annually is also available on request. A brief outline of the declarations of interest policy is described here and full details of the policy is available on the [Clarity Informatics website \(https://cks.clarity.co.uk/\)](https://cks.clarity.co.uk/). Declarations of interests of the authors are not routinely published, however competing interests of all those involved in the topic update or development are listed below. Competing interests include:

- Personal financial interests
- Personal family interest
- Personal non-financial interest
- Non-personal financial gain or benefit

Although particular attention is given to interests that could result in financial gains or losses for the individual, competing interests may also arise from academic competition or for political, personal, religious, and reputational reasons. An individual is not obliged to seek out knowledge of work done for, or on behalf of, the healthcare industry within the departments for which they are responsible if they would not normally expect to be informed.

## Who should declare competing interests?

Any individual (or organization) involved in developing, reviewing, or commenting on clinical content, particularly the recommendations should declare competing interests. This includes the authoring team members, expert advisers, external reviewers of draft topics, individuals providing feedback on published topics, and Editorial Steering Group members. Declarations of interest are completed annually for authoring team and editorial steering group members, and are completed at the start of the topic update and development process for external stakeholders.

## Competing interests declared for this topic:

None.

## Vitamin D deficiency in adults - treatment and prevention: Summary

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- Vitamin D is a fat soluble vitamin that regulates calcium and phosphate homeostasis and is therefore vital for musculoskeletal health.
- There are two main forms: vitamin D<sub>3</sub> (cholecalciferol) and D<sub>2</sub> (ergocalciferol).
  - Vitamin D<sub>3</sub> is synthesized in the skin by the action of sunlight.
  - Both vitamin D<sub>3</sub> and D<sub>2</sub> can be obtained from natural foods (which are limited and are mostly from animal sources), fortified foods, and food supplements.
- Dietary and cutaneous vitamin D are biologically inactive and require enzymatic conversion: firstly in the liver to 25-hydroxyvitamin D (25[OH]D – the main circulating metabolite), then to 1,25-hydroxyvitamin D (1,25[OH]<sub>2</sub>D – the active metabolite) in the kidneys and other tissues.
- Measurement of serum 25(OH)D concentrations is the best way of estimating vitamin D status. However, there is no clear consensus on the threshold concentration used to define vitamin D deficiency in adults.
- Evidence identified by the Scientific Advisory Committee on Nutrition (SACN) suggests that the risk of poor musculoskeletal health is increased at serum 25(OH)D concentration below 25 nmol/L.
- People with insufficient exposure to sunlight and those with darker skin are at higher risk of vitamin D deficiency. Other risk factors include nutritional deficiency, certain comorbidities (for example malabsorption syndromes), and the use of certain drugs (for example corticosteroids).
- Although vitamin D deficiency (25[OH]D less than 25 nmol/L) is common, universal screening is only recommended if:
  - There are musculoskeletal symptoms that can be attributed to vitamin D deficiency.
  - There is a clinical reason, for example if the person has had a fall, or prior to specific treatment where correcting vitamin D deficiency is appropriate.
- Management includes:
  - Considering the need for referral or seeking specialist advice, for example if a serious underlying condition (such as cancer) is suspected (referral is indicated).
  - Treating vitamin D deficiency (25[OH]D less than 25 nmol/L) with high-dose vitamin D for 6 -12 weeks (depending on the loading regimen used), followed by daily maintenance doses. For people with vitamin D insufficiency (25[OH]D 25-50 nmol/L), maintenance doses should be started without the use of loading doses.
  - Giving dietary advice (including on calcium intake) and lifestyle advice (including on safe sun exposure).
  - Following up the person to ensure correction of vitamin D deficiency and to assess for vitamin D toxicity (which usually manifests as hypercalcaemia).
- For people with sufficient vitamin D levels, advice on reducing the risk of vitamin D deficiency should be given, unless referral or seeking specialist advice is warranted, for example if there is persisting musculoskeletal pain.
- To prevent vitamin D deficiency:
  - All adults living in the UK should be advised to take a daily supplement containing 400 international units (10 micrograms) of vitamin D throughout the year, including in the winter months.
  - Dietary and lifestyle advice should also be given.

# Have I got the right topic?

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From age 18 years onwards.

This CKS topic is largely based on the National Osteoporosis Society (NOS) guideline *Vitamin D and bone health: a practical clinical guideline for patient management* [National Osteoporosis Society, 2013 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))], the Scientific Advisory Committee on Nutrition (SACN) report on *Vitamin D and health* [SACN, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))], and the National Institute for Health and Care Excellence (NICE) guidelines *Vitamin D: increasing supplement use in at-risk groups* [NICE, 2014 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))] and *Sunlight exposure: risks and benefits* [NICE, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))].

This CKS topic covers the treatment of people with vitamin D deficiency caused by inadequate sunlight exposure or nutritional deficiency. It also covers the prevention of vitamin D deficiency in adults.

This CKS topic does not cover the treatment or prevention of vitamin D deficiency in children. It also does not make detailed recommendations on how to manage people with vitamin D deficiency caused by a chronic disease or a drug treatment, or the management of people with osteoporosis or other bone disease.

There are separate CKS topics on [Vitamin D deficiency in children](#) ([/vitamin-d-deficiency-in-children](#)), [Antenatal care - uncomplicated pregnancy](#) ([/antenatal-care-uncomplicated-pregnancy](#)), [Breastfeeding problems](#) ([/breastfeeding-problems](#)), and [Osteoporosis - prevention of fragility fractures](#) ([/osteoporosis-prevention-of-fragility-fractures](#)).

The target audience for this CKS topic is healthcare professionals working within the NHS in the UK, and providing first contact or primary healthcare.

## How up-to-date is this topic?

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## Background information

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- [Scenario: Management of vitamin D deficiency or insufficiency in adults](#) ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!scenario](#)): covers the management of adults with confirmed vitamin D deficiency or insufficiency.
- [Scenario: Prevention of vitamin D deficiency](#) ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!scenario:1](#)): covers the prevention of vitamin D deficiency in adults.

## Prescribing information

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Important aspects of prescribing information relevant to primary healthcare are covered in this section specifically for the drugs recommended in this CKS topic. For further information on contraindications, cautions, drug interactions, and adverse effects, see the [electronic Medicines Compendium](http://www.medicines.org.uk/emc) (<http://www.medicines.org.uk/emc>) (eMC), or the [British National Formulary](https://bnf.nice.org.uk/) (<https://bnf.nice.org.uk/>) (BNF).

## Supporting evidence

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This CKS topic is largely based on the National Osteoporosis Society (NOS) guideline *Vitamin D and bone health: a practical clinical guideline for patient management* [National Osteoporosis Society, 2013 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))], the Scientific Advisory Committee on Nutrition (SACN) report on *Vitamin D and Health* [SACN, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))], and the National Institute for Health and Care Excellence (NICE) guidelines *Vitamin D: increasing supplement use in at-risk groups* [NICE, 2014 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))] and *Sunlight exposure: risks and benefits* [NICE, 2016 ([/vitamin-d-deficiency-in-adults-treatment-and-prevention#!references](#))]. Expert opinion in several local guidelines and review articles were also considered. The rationale for the individual recommendations is discussed in the relevant basis for recommendation sections.

## How this topic was developed

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This section briefly describes the processes used in developing and updating this topic. Further details on the full process can be found in the [About Us](#) (<http://cks.nice.org.uk/development>) section and on the [Clarity Informatics](https://clarity.co.uk/) (<https://clarity.co.uk/>) website.

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